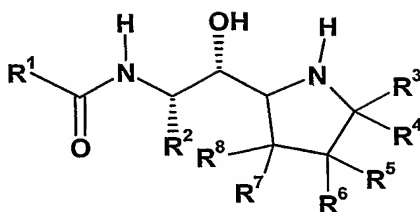


We Claim:

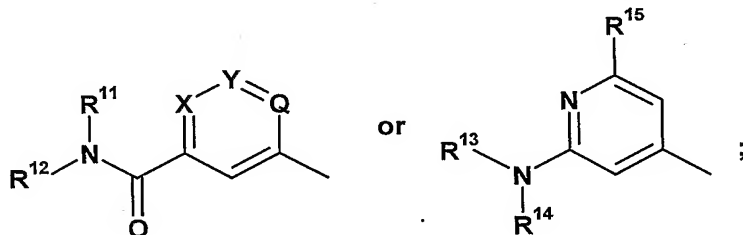
1. A compound of Formula I:



I

where:

R¹ is (C₃-C₇ cycloalkyl)₀₋₁(C₁-C₆ alkyl), (C₃-C₇ cycloalkyl)₀₋₁(C₂-C₆ alkenyl), (C₃-C₇ cycloalkyl)₀₋₁(C₂-C₆ alkynyl) or C₃-C₇ cycloalkyl, each optionally substituted with up to three groups independently selected from halo, hydroxy, thiol, cyano, trifluoromethyl, trifluoromethoxy, C₁-C₆ alkoxy, C₃-C₇ cycloalkoxy, oxo, and NR⁹R¹⁰, hydrogen,



biphenyl substituted with halo,

X is CH, N, or N⁺-O⁻;

Y is CR¹⁶, N, or N⁺-O⁻;

Q is CR¹⁷, N, or N⁺-O⁻;

R² is C₁-C₃ alkyl, benzyl optionally monosubstituted in the phenyl ring with a substituent selected from the group consisting of halo, C₁-C₆ alkoxy optionally substituted in the alkyl chain with C₃-C₇ cycloalkyl, and C₁-C₆ alkylthio optionally substituted in the alkyl chain with C₃-C₇ cycloalkyl, or benzyl optionally disubstituted in the phenyl ring with a first substituent independently selected from halo and a second substituent independently selected from halo, C₁-C₆ alkoxy optionally substituted in the alkyl chain with C₃-C₇ cycloalkyl, and C₁-C₆ alkylthio optionally substituted in the alkyl chain with C₃-C₇ cycloalkyl;

R³ is hydrogen or C₁-C₆ alkyl;

R⁴ is hydrogen, C₁-C₆ alkyl, or phenyl;

R^3 and R^4 taken together with the carbon to which they are attached form a C_3 - C_6 cycloalkyl ring;

R^5 is hydrogen, fluoro, trifluoromethyl, R^{32} , or phenyl optionally monosubstituted with C_1 - C_6 alkyl or C_1 - C_6 alkoxy;

5 R^6 is fluoro, hydroxy, *p*-toluenesulfonyloxy, R^{34} , $-\text{CH}_2\text{C}(\text{O})\text{R}^{35}$, or $-\text{OC}(\text{O})\text{NHR}^{36}$; or R^5 and R^6 taken together form $=\text{CHC}(\text{O})(\text{C}_1\text{-C}_4 \text{ alkoxy})$;

R^7 is hydrogen or fluoro; or R^6 and R^7 taken together form a bond;

R^8 is hydrogen or fluoro;

R^9 is hydrogen, C_1 - C_6 alkyl, or phenyl;

10 R^{10} is hydrogen, C_1 - C_6 alkyl, phenyl, $-\text{C}(\text{O})(\text{C}_1\text{-C}_6 \text{ alkyl})$, or $-\text{SO}_2(\text{C}_1\text{-C}_6 \text{ alkyl})$;

R^{11} and R^{12} are independently selected from the group consisting of methyl, ethyl, and propyl;

R^{13} is hydrogen or C_1 - C_6 alkyl;

R^{14} is C_3 - C_5 cycloalkyl, C_1 - C_6 alkyl, or $-\text{CH}_2\text{R}^{18}$;

15 R^{15} is $-\text{CF}_2\text{R}^{19}$, $-\text{OR}^{20}$, $-\text{CH}_2\text{C}(\text{O})\text{CH}_3$, $-\text{S}(\text{O})_{1-2}\text{R}^{21}$, $-\text{NR}^{22}\text{SO}_2\text{R}^{23}$, (C_1 - C_3 alkoxy)-carbonyl, phenyl optionally substituted with halo, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,1-dioxo-2,3,4,5-tetrahydroisothiazol-2-yl, or tetrazol-5-yl optionally substituted with C_1 - C_3 alkyl;

20 R^{16} is hydrogen, chloro, isobutyl, CH_2R^{24} , CF_2R^{25} , 1,1,1-trifluoro-2-hydroxyeth-2-yl, C_2 - C_4 alkenyl optionally substituted with one or two fluorine atoms, OR^{26} , $\text{C}(\text{O})\text{R}^{27}$, N(methyl)(methylsulfonyl), N(methyl)(acetyl), pyrrolidin-2-on-1-yl, methylsulfonyl, N,N-dimethylaminosulfonyl, phenyl optionally substituted with one or two substituents selected from the group consisting of hydroxymethyl, methoxy, fluoro, and methylsulfonyl, 1,3-dioxolan-2-yl, 1,3-dithiolan-2-yl, 1,3-oxathiolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithian-2-yl, pyridinyl, thiazolyl, oxazolyl, or 1,2,4-oxadiazolyl optionally substituted with methyl;

R^{17} is hydrogen or fluoro;

R^{18} is ethynyl or cyclopropyl;

R^{19} is hydrogen or methyl;

30 R^{20} is difluoromethyl or methanesulfonyl;

R^{21} is C_1 - C_4 alkyl, C_3 - C_6 cycloalkyl, phenyl, or $-\text{NR}^{30}\text{R}^{31}$;

R^{22} is hydrogen, C_1 - C_3 alkyl optionally substituted with up to 3 fluorine atoms, or C_3 - C_6 cycloalkyl;

R^{23} is C_1 - C_3 alkyl or C_3 - C_6 cycloalkyl;

R^{24} is fluoro, hydroxy, or C_1 - C_3 alkoxy;

5 R^{25} is hydrogen, phenyl, or furyl;

R^{26} is C_1 - C_3 alkyl optionally substituted with one or two fluorine atoms;

R^{27} is C_1 - C_3 alkyl, C_3 - C_5 cycloalkyl, C_2 - C_3 alkenyl, C_1 - C_3 alkoxy, $NR^{28}R^{29}$, pyrrolidin-1-yl optionally substituted with methyl or one or two fluorine atoms, piperidin-1-yl, phenyl, pyridinyl, or furyl;

10 R^{28} is hydrogen or methyl;

R^{29} is methyl, ethyl, or propyl;

R^{30} is hydrogen or methyl;

R^{31} is methyl; or

15 R^{30} and R^{31} taken together with the nitrogen atom to which they are attached form a pyrrolidine or piperidine ring;

R^{32} is C_1 - C_{10} alkyl optionally substituted with 1-6 fluorine atoms, oxo, or one or two hydroxy groups, C_2 - C_6 alkenyl, or $-(CH_2)_{0-3}-R^{33}$;

20 R^{33} is C_3 - C_7 cycloalkyl or phenyl each optionally substituted with one or two substituents independently selected from the group consisting of halo, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, hydroxy, trifluoromethyl, and trifluoromethoxy, or R^{33} is adamantyl;

R^{34} is hydrogen, R^{32} , or $-(CH_2)_{0-2}-OR^{32}$;

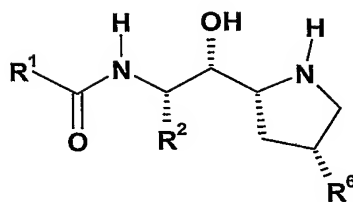
25 R^{35} is hydroxy, C_1 - C_6 alkoxy, or $NR^{37}R^{38}$ where R^{37} and R^{38} are independently hydrogen or C_1 - C_6 alkyl, or R^{37} and R^{38} , taken together with the nitrogen to which they are attached, form a piperidine ring optionally substituted with C_1 - C_6 alkyl, a homopiperidine ring, a morpholine ring, or a pyrrolidine ring optionally substituted with $(C_1$ - C_6 alkoxy)methyl;

R^{36} is C_1 - C_6 alkyl or adamantyl;

30 or a pharmaceutically acceptable salt thereof; provided that: a) no more than one of X, Y, and Q may be N or N^+-O^- ; and b) when X is CH, Y is CR^{16} , and Q is CR^{17} , then one of R^{16} and R^{17} is other than hydrogen.

2. A compound of Formula I(a):

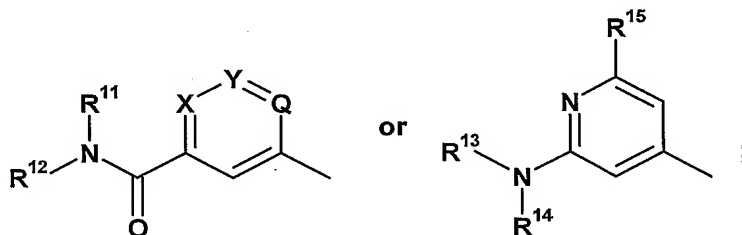
-182-



I(a)

where:

R^1 is (C₃-C₇ cycloalkyl)₀₋₁(C₁-C₆ alkyl), (C₃-C₇ cycloalkyl)₀₋₁(C₂-C₆ alkenyl), (C₃-C₇ cycloalkyl)₀₋₁(C₂-C₆ alkynyl) or C₃-C₇ cycloalkyl, each optionally substituted with up to three groups independently selected from halo, hydroxy, thiol, cyano, trifluoromethyl, trifluoromethoxy, C₁-C₆ alkoxy, C₃-C₇ cycloalkoxy, oxo, and NR⁹R¹⁰, hydrogen,



biphenyl substituted with halo,

X is CH, N, or N⁺-O⁻;

Y is CR¹⁶, N, or N⁺-O⁻;

Q is CR¹⁷, N, or N⁺-O⁻;

R^2 is C₁-C₃ alkyl, benzyl optionally monosubstituted in the phenyl ring with a substituent selected from the group consisting of halo, C₁-C₆ alkoxy optionally substituted in the alkyl chain with C₃-C₇ cycloalkyl, and C₁-C₆ alkylthio optionally substituted in the alkyl chain with C₃-C₇ cycloalkyl, or benzyl optionally disubstituted in the phenyl ring with a first substituent independently selected from halo and a second substituent independently selected from halo, C₁-C₆ alkoxy optionally substituted in the alkyl chain with C₃-C₇ cycloalkyl, and C₁-C₆ alkylthio optionally substituted in the alkyl chain with C₃-C₇ cycloalkyl;

R^6 is fluoro, hydroxy, p-toluenesulfonyloxy, R³⁴, -CH₂C(O)R³⁵, or -OC(O)NHR³⁶; or R⁵ and R⁶ taken together form =CHC(O)(C₁-C₄ alkoxy);

R⁹ is hydrogen, C₁-C₆ alkyl, or phenyl;

R¹⁰ is hydrogen, C₁-C₆ alkyl, phenyl, -C(O)(C₁-C₆ alkyl), or -SO₂(C₁-C₆ alkyl);

R^{11} and R^{12} are independently selected from the group consisting of methyl, ethyl, and propyl;

R^{13} is hydrogen or C_1 - C_6 alkyl;

R^{14} is C_3 - C_5 cycloalkyl, C_1 - C_6 alkyl, or $-CH_2R^{18}$;

5 R^{15} is $-CF_2R^{19}$, $-OR^{20}$, $-CH_2C(O)CH_3$, $-S(O)_{1-2}R^{21}$, $-NR^{22}SO_2R^{23}$, (C_1 - C_3 alkoxy)-carbonyl, phenyl optionally substituted with halo, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,1-dioxo-2,3,4,5-tetrahydroisothiazol-2-yl, or tetrazol-5-yl optionally substituted with C_1 - C_3 alkyl;

R^{16} is hydrogen, chloro, isobutyl, CH_2R^{24} , CF_2R^{25} , 1,1,1-trifluoro-2-hydroxyeth-2-yl, C_2 - C_4 alkenyl optionally substituted with one or two fluorine atoms, OR^{26} , $C(O)R^{27}$, N(methyl)(methylsulfonyl), N(methyl)(acetyl), pyrrolidin-2-on-1-yl, methylsulfonyl, N,N-dimethylaminosulfonyl, phenyl optionally substituted with one or two substituents selected from the group consisting of hydroxymethyl, methoxy, fluoro, and methylsulfonyl, 1,3-dioxolan-2-yl, 1,3-dithiolan-2-yl, 1,3-oxathiolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithian-2-yl, pyridinyl, thiazolyl, oxazolyl, or 1,2,4-oxadiazolyl optionally substituted with methyl;

R^{17} is hydrogen or fluoro;

R^{18} is ethynyl or cyclopropyl;

R^{19} is hydrogen or methyl;

20 R^{20} is difluoromethyl or methanesulfonyl;

R^{21} is C_1 - C_4 alkyl, C_3 - C_6 cycloalkyl, phenyl, or $-NR^{30}R^{31}$;

R^{22} is hydrogen, C_1 - C_3 alkyl optionally substituted with up to 3 fluorine atoms, or C_3 - C_6 cycloalkyl;

R^{23} is C_1 - C_3 alkyl or C_3 - C_6 cycloalkyl;

25 R^{24} is fluoro, hydroxy, or C_1 - C_3 alkoxy;

R^{25} is hydrogen, phenyl, or furyl;

R^{26} is C_1 - C_3 alkyl optionally substituted with one or two fluorine atoms;

R^{27} is C_1 - C_3 alkyl, C_3 - C_5 cycloalkyl, C_2 - C_3 alkenyl, C_1 - C_3 alkoxy, $NR^{28}R^{29}$, pyrrolidin-1-yl optionally substituted with methyl or one or two fluorine atoms, piperidin-1-yl, phenyl, pyridinyl, or furyl;

R^{28} is hydrogen or methyl;

R^{29} is methyl, ethyl, or propyl;

R^{30} is hydrogen or methyl;

R^{31} is methyl; or

R^{30} and R^{31} taken together with the nitrogen atom to which they are attached form a pyrrolidine or piperidine ring;

5 R^{32} is C_1 - C_{10} alkyl optionally substituted with 1-6 fluorine atoms, oxo, or one or two hydroxy groups, C_2 - C_6 alkenyl, or $-(CH_2)_{0-3}-R^{33}$;

R^{33} is C_3 - C_7 cycloalkyl or phenyl each optionally substituted with one or two substituents independently selected from the group consisting of halo, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, hydroxy, trifluoromethyl, and trifluoromethoxy, or R^{33} is adamantyl;

10 R^{34} is hydrogen, R^{32} , or $-(CH_2)_{0-2}-OR^{32}$;

R^{35} is hydroxy, C_1 - C_6 alkoxy, or $NR^{37}R^{38}$ where R^{37} and R^{38} are independently hydrogen or C_1 - C_6 alkyl, or R^{37} and R^{38} , taken together with the nitrogen to which they are attached, form a piperidine ring optionally substituted with C_1 - C_6 alkyl, a homopiperidine ring, a morpholine ring, or a pyrrolidine ring optionally substituted with
15 $(C_1$ - C_6 alkoxy)methyl;

R^{36} is C_1 - C_6 alkyl or adamantyl;

or a pharmaceutically acceptable salt thereof; provided that: a) no more than one of X, Y, and Q may be N or N^+-O^- ; and b) when X is CH, Y is CR^{16} , and Q is CR^{17} , then one of R^{16} and R^{17} is other than hydrogen.

20

3. The use of a compound of either of Claims 1 or 2 for the manufacture of a medicament for the treatment of Alzheimer's disease.

4. The use of a compound of either of Claims 1 or 2 for the manufacture of a
25 medicament for the prevention of the progression of mild cognitive impairment to Alzheimer's disease.

5. The use of a compound of either of Claims 1 or 2 for the manufacture of a medicament for the inhibition of BACE.

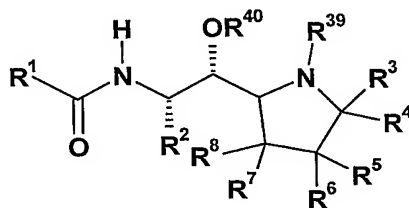
30

6. The use of a compound of either of Claims 1 or 2 for the manufacture of a medicament for treating a disease or condition capable of being improved or prevented by inhibition of BACE.

7. A pharmaceutical formulation adapted for the treatment of conditions resulting from excessive levels of A- β peptide comprising a compound of either of Claims 1 or 2 in combination with one or more pharmaceutically acceptable excipients, carriers, or diluents.

8. A pharmaceutical formulation comprising a compound of either of Claims 1 or 2, in combination with a pharmaceutically acceptable carrier, diluent, or excipient.

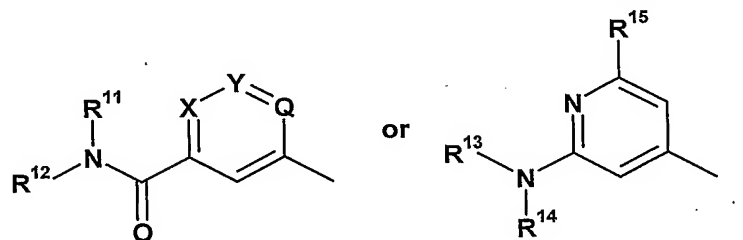
9. A compound of Formula III:



III

where:

R¹ is (C₃-C₇ cycloalkyl)₀₋₁(C₁-C₆ alkyl), (C₃-C₇ cycloalkyl)₀₋₁(C₂-C₆ alkenyl), (C₃-C₇ cycloalkyl)₀₋₁(C₂-C₆ alkynyl) or C₃-C₇ cycloalkyl, each optionally substituted with up to three groups independently selected from halo, hydroxy, thiol, cyano, trifluoromethyl, trifluoromethoxy, C₁-C₆ alkoxy, C₃-C₇ cycloalkoxy, oxo, and NR⁹R¹⁰, hydrogen,



biphenyl substituted with halo,

X is CH, N, or N⁺-O⁻;

Y is CR¹⁶, N, or N⁺-O⁻;

Q is CR¹⁷, N, or N⁺-O⁻;

R^2 is C_1 - C_3 alkyl, benzyl optionally monosubstituted in the phenyl ring with a substituent selected from the group consisting of halo, C_1 - C_6 alkoxy optionally substituted in the alkyl chain with C_3 - C_7 cycloalkyl, and C_1 - C_6 alkylthio optionally substituted in the alkyl chain with C_3 - C_7 cycloalkyl, or benzyl optionally disubstituted in the phenyl ring
5 with a first substituent independently selected from halo and a second substituent independently selected from halo, C_1 - C_6 alkoxy optionally substituted in the alkyl chain with C_3 - C_7 cycloalkyl, and C_1 - C_6 alkylthio optionally substituted in the alkyl chain with C_3 - C_7 cycloalkyl;

R^3 is hydrogen or C_1 - C_6 alkyl;

10 R^4 is hydrogen, C_1 - C_6 alkyl, or phenyl;

R^3 and R^4 taken together with the carbon to which they are attached form a C_3 - C_6 cycloalkyl ring;

R^5 is hydrogen, fluoro, trifluoromethyl, R^{32} , or phenyl optionally monosubstituted with C_1 - C_6 alkyl or C_1 - C_6 alkoxy;

15 R^6 is fluoro, hydroxy, *p*-toluenesulfonyloxy, R^{34} , $-\text{CH}_2\text{C}(\text{O})\text{R}^{35}$, or $-\text{OC}(\text{O})\text{NHR}^{36}$; or R^5 and R^6 taken together form $=\text{CHC}(\text{O})(\text{C}_1\text{-C}_4 \text{ alkoxy})$;

R^7 is hydrogen or fluoro; or R^6 and R^7 taken together form a bond;

R^8 is hydrogen or fluoro;

R^9 is hydrogen, C_1 - C_6 alkyl, or phenyl;

20 R^{10} is hydrogen, C_1 - C_6 alkyl, phenyl, $-\text{C}(\text{O})(\text{C}_1\text{-C}_6 \text{ alkyl})$, or $-\text{SO}_2(\text{C}_1\text{-C}_6 \text{ alkyl})$;

R^{11} and R^{12} are independently selected from the group consisting of methyl, ethyl, and propyl;

R^{13} is hydrogen or C_1 - C_6 alkyl;

R^{14} is C_3 - C_5 cycloalkyl, C_1 - C_6 alkyl, or $-\text{CH}_2\text{R}^{18}$;

25 R^{15} is $-\text{CF}_2\text{R}^{19}$, $-\text{OR}^{20}$, $-\text{CH}_2\text{C}(\text{O})\text{CH}_3$, $-\text{S}(\text{O})_{1-2}\text{R}^{21}$, $-\text{NR}^{22}\text{SO}_2\text{R}^{23}$, $(\text{C}_1\text{-C}_3 \text{ alkoxy})$ -carbonyl, phenyl optionally substituted with halo, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,1-dioxo-2,3,4,5-tetrahydroisothiazol-2-yl, or tetrazol-5-yl optionally substituted with C_1 - C_3 alkyl;

30 R^{16} is hydrogen, chloro, isobutyl, CH_2R^{24} ; CF_2R^{25} , 1,1,1-trifluoro-2-hydroxyeth-2-yl, C_2 - C_4 alkenyl optionally substituted with one or two fluorine atoms, OR^{26} , $\text{C}(\text{O})\text{R}^{27}$, $\text{N}(\text{methyl})(\text{methylsulfonyl})$, $\text{N}(\text{methyl})(\text{acetyl})$, pyrrolidin-2-on-1-yl, methylsulfonyl, N,N -dimethylaminosulfonyl, phenyl optionally substituted with one or two substituents

selected from the group consisting of hydroxymethyl, methoxy, fluoro, and methylsulfonyl, 1,3-dioxolan-2-yl, 1,3-dithiolan-2-yl, 1,3-oxathiolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithian-2-yl, pyridinyl, thiazolyl, oxazolyl, or 1,2,4-oxadiazolyl optionally substituted with methyl;

- 5 R¹⁷ is hydrogen or fluoro;
 R¹⁸ is ethynyl or cyclopropyl;
 R¹⁹ is hydrogen or methyl;
 R²⁰ is difluoromethyl or methanesulfonyl;
 R²¹ is C₁-C₄ alkyl, C₃-C₆ cycloalkyl, phenyl, or -NR³⁰R³¹;
10 R²² is hydrogen, C₁-C₃ alkyl optionally substituted with up to 3 fluorine atoms, or C₃-C₆ cycloalkyl;
 R²³ is C₁-C₃ alkyl or C₃-C₆ cycloalkyl;
 R²⁴ is fluoro, hydroxy, or C₁-C₃ alkoxy;
 R²⁵ is hydrogen, phenyl, or furyl;
15 R²⁶ is C₁-C₃ alkyl optionally substituted with one or two fluorine atoms;
 R²⁷ is C₁-C₃ alkyl, C₃-C₅ cycloalkyl, C₂-C₃ alkenyl, C₁-C₃ alkoxy, NR²⁸R²⁹, pyrrolidin-1-yl optionally substituted with methyl or one or two fluorine atoms, piperidin-1-yl, phenyl, pyridinyl, or furyl;
 R²⁸ is hydrogen or methyl;
20 R²⁹ is methyl, ethyl, or propyl;
 R³⁰ is hydrogen or methyl;
 R³¹ is methyl; or
 R³⁰ and R³¹ taken together with the nitrogen atom to which they are attached form a pyrrolidine or piperidine ring;
25 R³² is C₁-C₁₀ alkyl optionally substituted with 1-6 fluorine atoms, oxo, or one or two hydroxy groups, C₂-C₆ alkenyl, or -(CH₂)₀₋₃-R³³;
 R³³ is C₃-C₇ cycloalkyl or phenyl each optionally substituted with one or two substituents independently selected from the group consisting of halo, C₁-C₆ alkyl, C₁-C₆ alkoxy, hydroxy, trifluoromethyl, and trifluoromethoxy, or R³³ is adamantyl;
30 R³⁴ is hydrogen, R³², or -(CH₂)₀₋₂-OR³²;
 R³⁵ is hydroxy, C₁-C₆ alkoxy, or NR³⁷R³⁸ where R³⁷ and R³⁸ are independently hydrogen or C₁-C₆ alkyl, or R³⁷ and R³⁸, taken together with the nitrogen to which they

are attached, form a piperidine ring optionally substituted with C₁-C₆ alkyl, a homopiperidine ring, a morpholine ring, or a pyrrolidine ring optionally substituted with (C₁-C₆ alkoxy)methyl;

R³⁶ is C₁-C₆ alkyl or adamantyl;

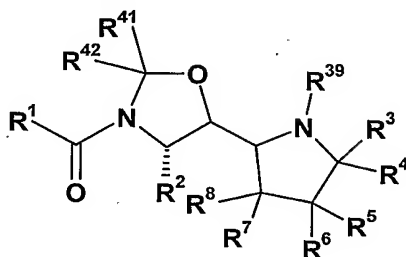
5 R³⁹ is hydrogen or a nitrogen protecting group;

R⁴⁰ is hydrogen or an oxygen protecting group;

or an acid addition salt thereof; provided that: a) no more than one of X, Y, and Q may be N or N⁺-O⁻; b) when X is CH, Y is CR¹⁶, and Q is CR¹⁷, then one of R¹⁶ and R¹⁷ is other than hydrogen; and c) at least one of R³⁹ and R⁴⁰ is other than hydrogen.

10

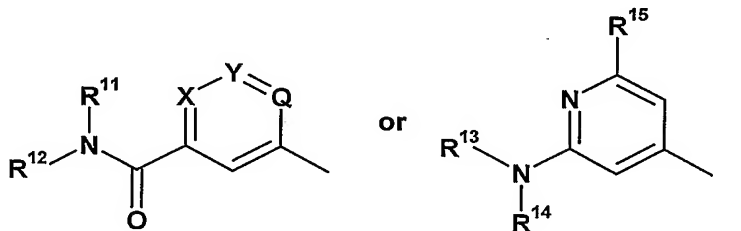
10. A compound of Formula IV:



IV

where:

15 R¹ is (C₃-C₇ cycloalkyl)₀₋₁(C₁-C₆ alkyl), (C₃-C₇ cycloalkyl)₀₋₁(C₂-C₆ alkenyl), (C₃-C₇ cycloalkyl)₀₋₁(C₂-C₆ alkynyl) or C₃-C₇ cycloalkyl, each optionally substituted with up to three groups independently selected from halo, hydroxy, thiol, cyano, trifluoromethyl, trifluoromethoxy, C₁-C₆ alkoxy, C₃-C₇ cycloalkoxy, oxo, and NR⁹R¹⁰, hydrogen,



biphenyl substituted with halo,

20 X is CH, N, or N⁺-O⁻;

Y is CR¹⁶, N, or N⁺-O⁻;

Q is CR¹⁷, N, or N⁺-O⁻;

R^2 is C_1 - C_3 alkyl, benzyl optionally monosubstituted in the phenyl ring with a substituent selected from the group consisting of halo, C_1 - C_6 alkoxy optionally substituted in the alkyl chain with C_3 - C_7 cycloalkyl, and C_1 - C_6 alkylthio optionally substituted in the alkyl chain with C_3 - C_7 cycloalkyl, or benzyl optionally disubstituted in the phenyl ring
 5 with a first substituent independently selected from halo and a second substituent independently selected from halo, C_1 - C_6 alkoxy optionally substituted in the alkyl chain with C_3 - C_7 cycloalkyl, and C_1 - C_6 alkylthio optionally substituted in the alkyl chain with C_3 - C_7 cycloalkyl;

R^3 is hydrogen or C_1 - C_6 alkyl;

10 R^4 is hydrogen, C_1 - C_6 alkyl, or phenyl;

R^3 and R^4 taken together with the carbon to which they are attached form a C_3 - C_6 cycloalkyl ring;

R^5 is hydrogen, fluoro, trifluoromethyl, R^{32} , or phenyl optionally monosubstituted with C_1 - C_6 alkyl or C_1 - C_6 alkoxy;

15 R^6 is fluoro, hydroxy, p-toluenesulfonyloxy, R^{34} , $-\text{CH}_2\text{C}(\text{O})\text{R}^{35}$, or $-\text{OC}(\text{O})\text{NHR}^{36}$; or R^5 and R^6 taken together form $=\text{CHC}(\text{O})(\text{C}_1\text{-C}_4 \text{ alkoxy})$ or oxo;

R^7 is hydrogen or fluoro; or R^6 and R^7 taken together form a bond;

R^8 is hydrogen or fluoro;

R^9 is hydrogen, C_1 - C_6 alkyl, or phenyl;

20 R^{10} is hydrogen, C_1 - C_6 alkyl, phenyl, $-\text{C}(\text{O})(\text{C}_1\text{-C}_6 \text{ alkyl})$, or $-\text{SO}_2(\text{C}_1\text{-C}_6 \text{ alkyl})$;

R^{11} and R^{12} are independently selected from the group consisting of methyl, ethyl, and propyl;

R^{13} is hydrogen or C_1 - C_6 alkyl;

R^{14} is C_3 - C_5 cycloalkyl, C_1 - C_6 alkyl, or $-\text{CH}_2\text{R}^{18}$;

25 R^{15} is $-\text{CF}_2\text{R}^{19}$, $-\text{OR}^{20}$, $-\text{CH}_2\text{C}(\text{O})\text{CH}_3$, $-\text{S}(\text{O})_{1-2}\text{R}^{21}$, $-\text{NR}^{22}\text{SO}_2\text{R}^{23}$, $(\text{C}_1\text{-C}_3 \text{ alkoxy})$ -carbonyl, phenyl optionally substituted with halo, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,1-dioxo-2,3,4,5-tetrahydroisothiazol-2-yl, or tetrazol-5-yl optionally substituted with C_1 - C_3 alkyl;

30 R^{16} is hydrogen, chloro, isobutyl, CH_2R^{24} , CF_2R^{25} , 1,1,1-trifluoro-2-hydroxyeth-2-yl, C_2 - C_4 alkenyl optionally substituted with one or two fluorine atoms, OR^{26} , $\text{C}(\text{O})\text{R}^{27}$, N(methyl)(methylsulfonyl), N(methyl)(acetyl), pyrrolidin-2-on-1-yl, methylsulfonyl, N,N-dimethylaminosulfonyl, phenyl optionally substituted with one or two substituents

selected from the group consisting of hydroxymethyl, methoxy, fluoro, and methylsulfonyl, 1,3-dioxolan-2-yl, 1,3-dithiolan-2-yl, 1,3-oxathiolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithian-2-yl, pyridinyl, thiazolyl, oxazolyl, or 1,2,4-oxadiazolyl optionally substituted with methyl;

5 R^{17} is hydrogen or fluoro;

R^{18} is ethynyl or cyclopropyl;

R^{19} is hydrogen or methyl;

R^{20} is difluoromethyl or methanesulfonyl;

R^{21} is C_1 - C_4 alkyl, C_3 - C_6 cycloalkyl, phenyl, or $-NR^{30}R^{31}$;

10 R^{22} is hydrogen, C_1 - C_3 alkyl optionally substituted with up to 3 fluorine atoms, or C_3 - C_6 cycloalkyl;

R^{23} is C_1 - C_3 alkyl or C_3 - C_6 cycloalkyl;

R^{24} is fluoro, hydroxy, or C_1 - C_3 alkoxy;

R^{25} is hydrogen, phenyl, or furyl;

15 R^{26} is C_1 - C_3 alkyl optionally substituted with one or two fluorine atoms;

R^{27} is C_1 - C_3 alkyl, C_3 - C_5 cycloalkyl, C_2 - C_3 alkenyl, C_1 - C_3 alkoxy, $NR^{28}R^{29}$, pyrrolidin-1-yl optionally substituted with methyl or one or two fluorine atoms, piperidin-1-yl, phenyl, pyridinyl, or furyl;

R^{28} is hydrogen or methyl;

20 R^{29} is methyl, ethyl, or propyl;

R^{30} is hydrogen or methyl;

R^{31} is methyl; or

R^{30} and R^{31} taken together with the nitrogen atom to which they are attached form a pyrrolidine or piperidine ring;

25 R^{32} is C_1 - C_{10} alkyl optionally substituted with 1-6 fluorine atoms, oxo, or 1 or 2 hydroxy groups, C_2 - C_6 alkenyl, or $-(CH_2)_{0-3}-R^{33}$;

R^{33} is C_3 - C_7 cycloalkyl or phenyl each optionally substituted with one or two substituents independently selected from the group consisting of halo, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, hydroxy, trifluoromethyl, and trifluoromethoxy, or R^{33} is adamantyl;

30 R^{34} is hydrogen, R^{32} , or $-(CH_2)_{0-2}-OR^{32}$;

R^{35} is hydroxy, C_1 - C_6 alkoxy, or $NR^{37}R^{38}$ where R^{37} and R^{38} are independently hydrogen or C_1 - C_6 alkyl, or R^{37} and R^{38} , taken together with the nitrogen to which they

are attached, form a piperidine ring optionally substituted with C₁-C₆ alkyl, a homopiperidine ring, a morpholine ring, or a pyrrolidine ring optionally substituted with (C₁-C₆ alkoxy)methyl;

R³⁶ is C₁-C₆ alkyl or adamantyl;

5 R³⁹ is hydrogen or a nitrogen protecting group;

R⁴¹ and R⁴² are independently selected from methyl, ethyl, and propyl;

or an acid addition salt thereof; provided that no more than one of X, Y, and Q may be N or N⁺-O⁻.